

Amendments to the Specification

The additions have been indicated by underlining. Text that originally was emphasized with underlining has been modified to bold font.

Please replace the second paragraph on page 18 with the following amended paragraph:

The epitope region of HIV I or HIV II or HIV subtype O amino acid sequence is particularly preferable selected from the group of amino acid sequences:

NNTRKSISIG PGRAFYT	(I) [SEQ ID NO: 1]
NTTRSISIGP GRAFYT	(II) [SEQ ID NO: 2]
IDIQEERRMR IGGPGMAWYS	(III) [SEQ ID NO: 3]
QARILAVERY LKDQQQLLGIW GASG	(IV) [SEQ ID NO: 4]
LGIWGCSGKL ICTTAVPWNA SWS	(V) [SEQ ID NO: 5]
KDQQQLLGIWG SSGKL	(VI) [SEQ ID NO: 6]
ALETLLQNQQ LLSLW	(VII) [SEQ ID NO: 7]
LSLGCKGKL VCYTS	(VIII) [SEQ ID NO: 8]
WGIRQLRARL LALETLLQN	(IX) [SEQ ID NO: 9] and
QAQLNSWGCA FRQVCHTTVP WPNDSLTT	(X) [SEQ ID NO: 10]

or partial sequences thereof which have a length of at least 6 and preferably of at least 8 amino acids.

Please replace the paragraph which spans page 18 fourth paragraph through page 19 first paragraph with the following amended paragraph:

The epitope region of HCV amino acid sequences is preferably selected from the group of the amino acid sequences:

SRRFAQALPV WARPD	(XI) [SEQ ID NO: 11]
PQDVKFPGGG QIVGGV	(XII) [SEQ ID NO: 12]
EEASQHLPYI EQ	(XIII) [SEQ ID NO: 13]
QKALGLLQT	(XIV) [SEQ ID NO: 14]
SRGNHVSPTH YVPESDAA	(XV) [SEQ ID NO: 15]
PQRKNKRNTN RRPQDVKFPG	
GGQIVGVV	(XVI) [SEQ ID NO: 16] and
AWYELTPAET TVRLRAYMNT PGLPV	(XVII) [SEQ ID NO: 17]

or partial sequences thereof which have a length of at least 6 and preferably at least 8 amino acids. The sequence XI is derived from the NS5 region, the sequences XII and XVI from the Core region, the sequences XIII, XIV and XV from the NS4 region and the sequence XVII is derived from the NS3 region of HCV. The amino acid sequences XI to XVII are also shown in the sequence protocols SEQ ID NO. 11 to SEQ ID NO. 17.

Please replace the paragraph which spans page 21 third paragraph through page 22 first paragraph with the following amended paragraph:

The present invention is further described by the following examples, sequence protocols and figures.

SEQ ID NO. 1: shows the amino acid sequence of an epitope from the gp120 region of HIV I;

SEQ ID NO. 2: shows the amino acid sequence of a further epitope from the gp120 region of HIV I;

- SEQ ID NO. 3: shows the amino acid sequence of a further epitope from the gp120 region of HIV I, subtype O;
- SEQ ID NO. 4: shows the amino acid sequence of an epitope from the gp41 region of HIV I;
- SEQ ID NO. 5: shows the amino acid sequence of a further epitope from the gp41 region of HIV I;
- SEQ ID NO. 6: shows the amino acid sequence of yet a further epitope from the gp41 region of HIV I;
- SEQ ID NO. 7: shows the amino acid sequence of an epitope from the gp41 region of HIV I, subtype O;
- SEQ ID NO. 8: shows the amino acid sequence of a further epitope from the gp41 region of HIV I, subtype O;
- SEQ ID NO. 9: shows the amino acid sequence of yet a further epitope from the gp41 region of HIV I, subtype O;
- SEQ ID NO. 10: shows the amino acid sequence of an epitope from the gp32 region of HIV II;
- SEQ ID NO. 11: shows the amino acid sequence of an epitope from the NS5 region of HCV;
- SEQ ID NO. 12: shows the amino acid sequence of an epitope from the Core region of HCV;
- SEQ ID NO. 13: shows the amino acid sequence of an epitope from the NS4 region of HCV;
- SEQ ID NO. 14: shows the amino acid sequence of a further epitope from the NS4 region of HCV;

- SEQ ID NO. 15: shows the amino acid sequence of yet a further epitope from the NS4 region of HCV;
- SEQ ID NO. 16: shows the amino acid sequence of a further epitope from the Core region of HCV and
- SEQ ID NO. 17: shows the amino acid sequence of an epitope from the NS3 region of HCV;
- Figure 1: shows the amino acid sequence of the recombinant HIV p24 antigen, [SEQ ID NO: 77]
- Figure 2: shows a comparison of the measured signals in a double antigen bridge test when using a monomeric and a multimeric ruthenylated HIV-gp120 antigen and
- Figure 3: shows a comparison of the measured signals in a double antigen bridge test when using a monomeric and a multimeric biotinylated HIV-gp41 antigen.

Please replace Table 2a in the sixth paragraph on page 26 with the following amended table:

Table 2a: SH-activated linear peptides

Table 2a: SH-activated linear peptides

gp41/1	CUZU-WGIRQLRARLLALETLLQN <u>[SEQ ID NO: 18]</u>
gp41/2	CUZU-LSLWGCKGKLVCYTS <u>[SEQ ID NO: 19]</u>
gp41/4	CUZU-ALETLLQNQQLLSW <u>[SEQ ID NO: 20]</u>
gp120	CUZU-IDIQEMRIGPMAWYS <u>[SEQ ID NO: 21]</u>

Please replace Table 2b in the first paragraph on page 27 with the following amended table:

Table 2b: Digoxigenin-labeled linear peptides

Table 2b: Digoxigenin-labeled linear peptides

gp120	Digoxigenin-3-cme-UZU-NNTRKSISIGPGRAYT [SEQ ID NO: 22] Digoxigenin-3-cme-UZ-NTTRSISIGPGRAY [SEQ ID NO: 23] Digoxigenin-3-cme-UZU-IDIQEERRMRIGPGMAWYS [SEQ ID NO: 24]
gp41/1	Digoxigenin-3-cme-UZU-AVERYLKDQQQLLGW [SEQ ID NO: 25] Digoxigenin-3-cme-ZUZU-AVERYLKDQQQLLGW [SEQ ID NO: 26] Digoxigenin-3-cme-UZ-QARILAVERYLKDQQQLLGW [SEQ ID NO: 27] Digoxigenin-3-cme-ZGGGG-QARILAVERYLKDQQQLLGW [SEQ ID NO: 28] Digoxigenin-3-cme-UZU-WGIRQLRARLLAETLLQN [SEQ ID NO: 29]
gp41/2	Digoxigenin-3-cme-UZU-LGIWGCSGKLICTTAV [SEQ ID NO: 30] LGIWGCSGK-(cme-3-digoxigenin)-LICTTAV [SEQ ID NO: 31] Digoxigenin-3-cme-UZU-LGIWGCSGK-(cme-3-digoxigenin)-LICTTAV [SEQ ID NO: 32] Digoxigenin-3-cme-ZU-GCSGKLICTTAVPWNASWS [SEQ ID NO: 33] GCSGK-(cme-3-digoxigenin)-LICTTAVPWNASWS [SEQ ID NO: 34] GCSGKLICTTAVPWNASWSK (cme-3-digoxigenin) G [SEQ ID NO: 35] Digoxigenin-3-cme-UZU-LSLWGCKGKLVCYTS [SEQ ID NO: 36]
gp41/3	Digoxigenin-3-cme-UZU-KDQQQLLGW [SEQ ID NO: 37]

gp41/4	Digoxigenin-3-cme-UZU-ALETLLQNQQLSLW [SEQ ID NO: 38]
gp32	Digoxigenin-3-cme-Z-NSWGCAFRQVCHTT [SEQ ID NO: 39]

Please replace Table 2c in the first paragraph on page 28 with the following amended table:

Table 2c: Ruthenylated linear peptides

Table 2c: Ruthenylated linear peptides

gp120	BPRu-UZU-NNTRKSISIGPGRAFYT [SEQ ID NO: 40] BPRu-UZ-NTTRSISIGRGRAFY [SEQ ID NO: 41] BPRu-(ethyleneglycol)-UZ-NTTRSISIGPGRAFY [SEQ ID NO: 42] PBRu-UZU-IDIQEERRMRIGPGMAWYS [SEQ ID NO: 43]
gp41/1	PBRu-UZU-AVERYLKDQQQLLGW [SEQ ID NO: 44] BPRu-UGGG-QARILAVERYLKDQQQLLGWASG [SEQ ID NO: 45] BPRu-GGGG-QARILAVERYLKDQQQLLGWASG [SEQ ID NO: 46] BPRu-UZU-WGIRQLRARLLAETLLQN [SEQ ID NO: 47]
gp41/2	BPRu-UZU-LGIWGCSGKLICTTAV [SEQ ID NO: 48] BPRu-UGGG-GCSGKLICTTAVPWNASWS [SEQ ID NO: 49] (GCSGKLICTTAVPWNASWS)K-(BPRu) [SEQ ID NO: 50]
gp41/3	BPRu-UZU-KDQQQLLGWSSGKL [SEQ ID NO: 51]

gp41/4	BPRu-UZU-ALETLLQNALLSLW [SEQ ID NO: 52]
gp32	BPRu-UZU-NSWGCAFRQVCHTT [SEQ ID NO: 53] BPRu-GGG-QAQLNSWGCAFRQVCHTTVPWPNDL [SEQ ID NO: 54]

Please replace Table 3a in the fourth paragraph on page 28 with the following amended table:

Table 3a: SH-activated linear peptides

Table 3a: SH-activated linear peptides

NS4/3	C-UZ-SRGNHVSPTHYVPESDAA [SEQ ID NO: 55]
-------	---

Please replace Table 3b in the first paragraph on page 29 with the following amended table:

Table 3b: Hapten-labeled linear peptides

Table 3b: Hapten-labeled linear peptides

NS5/1	digoxigenin-3-cme-UZU-SRRFAQALPVWARP [SEQ ID NO: 56]
Core2m	digoxigenin-3-cme-U-PQDVKFPGGGQIVGGV [SEQ ID NO: 57]
NS4/1	digoxigenin-3-cme-UU-Nle-EEASQHLPYIEQ [SEQ ID NO: 58]
NS4/2	digoxigenin-3-cme-UU-QKALGLLQT [SEQ ID NO: 59]

NS4/3	digoxigenin-3-cme-UZU-SRGNHVSPTHYVPESDAA [SEQ ID NO: 60]
Core1	digoxigenin-3-cme-UZU-KNKRNTNRR [SEQ ID NO: 61]
Core1+2	digoxigenin-3-cme-U-PQRKNKRNTNRRPQDVKFPGGGQIVGVV [SEQ ID NO: 62]
NS3/1	digoxigenin-3-cme-UZ-AWYELTPAETTVRLRAYMNTPGLPV [SEQ ID NO: 63]

Please replace the table in the second paragraph on page 29 with the following amended table:

Example 3c: Ruthenylated linear peptides

Example 3c: Ruthenylated linear peptides

Core1	BPRu-GGGG-KNKRNTNRR [SEQ ID NO: 64]
Core1+2	BPRu-UZU-KNKRNTNRRPQDVKFPGGGQIVGGV [SEQ ID NO: 65]
NS4/1+2	BPRu-UZU-SQHLPYIEQG-NleNle-LAEQFKQQALGLLQT [SEQ ID NO: 66]
NS4/3m	BPRu-UZ-SRGNHVSPTHYVPESDAA [SEQ ID NO: 67]
NS5/1	BPRu-UZ-SRRFAQALPVWARPD [SEQ ID NO: 68]

Core1+2+3	BPRz-UZ-KNKRNTNRRPQDVKFPGGGQIVGGVLLPRR [SEQ ID NO: 69]
Core1m	BPRu-UZ-NPKPQKKNRNTNRR [SEQ ID NO: 70]
Core3m	BPRu-UZ-GQIVGGVYLLPRRGPRLG [SEQ ID NO: 71]
Core2m	BPRu-UZ-PQDVKFPGGGQIVGGV [SEQ ID NO: 72]
NS4/3m-I	BPRuz-UZU-SRGNHVSPTHYVPESDAA [SEQ ID NO: 73]
NS4/1	BPRu-UZU-SQHLPYIEQ [SEQ ID NO: 74]

Please replace the paragraph which spans page 35 sixth paragraph through page 36

first paragraph with the following amended paragraph:

Various variants of biotinylated polyhaptens were used in a double-antigen immunoassay in combination with a monomeric digoxygenylated hapten and namely with the same molar amount of biotinylated or digoxygenylated hapten. The amino acid sequence NNTRKSISIGPGRAFYT [SEQ ID NO: 1] from the gp120 region of HIV was used as the epitope. The haptens were synthesized as described in examples 1 and 2. The relative reactivity of native anti-HIV sera with the various biotinylated polyhaptens was standardized to the reactivity of sera with the corresponding biotinylated monomeric hapten (= 100% reactivity).

Please replace the paragraph which spans page 36 fourth paragraph through page 37
first paragraph with the following amended paragraph:

In the case of one epitope from the NS4 region of HCV (sequence SRGNHVSPTHYVPESDAA [SEQ ID NO: 15] the combination of a monomeric biotinylated antigen and a monomeric ruthenylated antigen was compared with the combination of multimeric branched biotinylated antigen (see Table 3d, line 2) and a

monomeric ruthenylated antigen in a bridge test. The signal differentiation was determined i.e. the ratio in the measured signal between positive and negative samples. A higher signal differentiation means a better sensitivity. When using a multimeric biotinylated antigen a signal differentiation of 386 compared to a signal differentiation of only 208 for the combination of both monomeric antigens was obtained.

Please replace the second paragraph on page 37 the following amended paragraph:

A double antigen bridge test was carried out correspondingly using an antigen sequence from the gp120 region of HIV. The epitope used has the amino acid sequence NTTRSI SIGPGRAY [SEQ ID NO: 2]. A combination of a monomeric biotinylated and a monomeric ruthenylated antigen was compared with a combination of a multimeric branched biotinylated antigen (see Table 2d, line 2) and a multimeric ruthenylated antigen (see Table 2d, line 4). In a test using the combination of the two multimeric antigens a signal differentiation between a positive and negative sample of 12 was found. In contrast the combination of both monomeric antigens only has a signal differentiation of 10.